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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,653	11/14/2003	Molly Accola	FORS-08453	1634

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Casimir Jones, S.C.
440 Science Drive
Suite 203
Madison, WI 53711

EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/713,653	ACCOLA ET AL.	
	Examiner	Art Unit	
	JEANINE A. GOLDBERG	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,30,33,36-38,43,44 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30,33,36-38,43,44 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/08; 10/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This action is in response to the papers filed March 6, 2009. Currently, claims 28, 30, 33, 36-38, 43-44, 47 are pending.

2. All arguments have been thoroughly reviewed but are deemed non-persuasive for the reasons which follow.

3. Any objections and rejections not reiterated below are hereby withdrawn.

4. This action is FINAL.

Election/Restrictions

5. Applicant's election without traverse of Group II, Claims 28-35 and newly added Claims 36-47 in the paper filed August 21, 2006 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Priority

6. This application claims priority to several provisional applications and as a CIP of 10/371,913, filed February 21, 2003.

Drawings

7. The drawings are acceptable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 28, 30, 33, 36-38, 43-44, 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ohnishi et al. (J. Hum. Genet. Vol 46, pages 471-477, 2001) in view of The Cystic Fibrosis Mutation Database (http://www.genet.sickkids.on.ca/cftr/app) and Fors et al. (Pharmacogenomics, Vol. 1, No. 2, pages 219-229, 2000), Mein et al. (Genome Research, Vol. 10, pages 330-343, 2000) and Rameckers et al. (Naturwissenschaften, Vol 84, pages 259-262, 1997).

Ohnishi et al. teaches a high-throughput SNP typing system for genome-wide association studies. Ohnishi teaches combining Invader assay with multiplex PCR (abstract). Ohnishi teaches amplifying 100 genomic DNA fragments in a single tube and analyzed each SNP with the Invader assay. Ohnishi teaches that the results indicate the feasibility of undertaking genome-wide association studies using blood

samples of only 5-10ml (abstract). Ohnishi teaches that primers were designed, multiplex amplifications were performed and PCR was performed for 35 cycles. Ohnishi teaches that after amplification was performed using 50ng of genomic DNA, the Invader assay was performed with unique probes corresponding to each SNP allele (page 472, col. 2). Ohnishi teaches that a set of 24 SNP loci was performed and the sequencing results were 100% identical to the genotyping data obtained by the Invader assays. Ohnishi teaches numerous benefits of multiplex analysis including reduced cost, significant reduction in the amount of genomic DNA required and savings in time (page 474, col. 1-2).

Ohnishi does not specifically teach amplifying nucleic acid with less than 25 cycles and using 20 CFTR alleles for analysis of SNPs and deletions.

However, the cystic fibrosis mutation databases teaches the collection of mutations in the CFTR gene. There are currently **1542** mutations listed in this CFTR mutation database. The mutations include SNPs and deletions. The most common F508 mutation is a deletion.

Moreover, Fors teaches large-scale SNP scoring from unamplified genomic DNA. Fors teaches the Invader assay offers a simple diagnostic platform to detect single nucleotide changes with high specificity and sensitivity from unamplified, genomic DNA. The Invader assay uses a structure-specific 5' nuclease (or flap endonuclease) to cleave sequence-specific structures in each of two cascading reactions. The cleavage structure forms when two synthetic oligonucleotide probes hybridize in tandem to a target. Fors teaches that the signal amplification permits identification of single base

changes directly from genomic DNA without prior amplification (abstract). The Invader technology is in routine use today for high-throughput SNP screening. The technology involves a simple, cascading reaction that can detect mutations and SNPs directly from unamplified genomic DNA or RNA in a homogeneous, isothermal, FRET-based format (page 222). Figure 1 illustrates the schematic of the Invader assay which contains various oligonucleotides including an oligonucleotide which comprises various 5' and 3' positions that do not hybridize to target sequences. The technology is readily adapted to different sequences since the unlabeled analyte-specific oligonucleotides used in the primary reaction; no new dye-labeled oligonucleotides are needed (page 223, col. 1). This creates a streamlined approach to creating new assays allows rapid and accurate synthesis, purification and quantification of new SNP assay sets.

Similarly, Mein teaches evaluating SNPs and an insertion deletion polymorphisms using PCR with Invader. Mein further teaches the benefits of automating the assay for savings on labor costs.

Further, Rameckers et al reviews "how many cycles does a PCR need?" Rameckers reviews the state of the art and analyzes the calculations of the number of PCR cycles (page 259, col. 2-3). Rameckers teaches the community of PCR users knows from experience that the efficiency of a PCR amplification is 1.00 only in theory (page 259, col. 3). Rameckers teaches formula 1 which is used to describe the PCR process. The skill in the art at the time the invention was made was extremely high. Analysis of the cycle numbers and parameters for PCR was routine. Rameckers illustrates situations using 17 cycles for 100,000 targets.

Therefore, it would have been prima facie obvious at the time the invention was made to generate an invader multiplex method, as taught by Ohnishi, for Cystic Fibrosis SNPs and deletions, as taught by CFMXB, using the PCR Invader technology design of Fors and Mein with less than 17 cycles, as taught by Rameckers. The ordinary artisan would have been motivated to have applied the PCR-Invader assay to CFTR gene SNPs and deletion mutations because CFTR gene mutations are diagnostic of Cystic fibrosis which is a debilitating disease. The art clearly illustrates the ability of Invader to detect both SNPs and deletion mutations. Moreover, Ohnishi specifically teaches the benefits of the PCR-invader assay as allowing multiplex analysis with the expected benefits of saving time, sample and cost. Thus, detecting multiple mutations simultaneously, including over 30 mutations would have been obvious at the time the invention was made given the number or CF mutations in the CFTR gene.

The ordinary artisan would have been motivated to have used 17 cycles or fewer as taught by Rameckers. Although Ohnishi suggests the use of 35 cycles for PCR amplification, the skilled artisan, given the teachings of Rameckers would have appreciated that exponential amplification introduces possibilities of amplicon cross contamination. As noted in *In re Aller*, 105 USPQ 233 at 235, "More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." MPEP 2144.05 continues to state, "A range can be disclosed in multiple prior art references instead of in a single prior art reference depending on the specific facts of the case. Iron Grip Barbell Co., Inc. v. USA Sports, Inc., 392 F.3d 1317, 1322, 73 USPQ2d 1225, 1228

(Fed. Cir. 2004). The patent claim at issue was directed to a weight plate having 3 elongated openings that served as handles for transporting the weight plate. Multiple prior art patents each disclosed weight plates having 1, 2 or 4 elongated openings. 392 F.3d at 1319, 73 USPQ2d at 1226. The court stated that the claimed weight plate having 3 elongated openings fell within the "range" of the prior art and was thus presumed obvious. 392 F.3d at 1322, 73 USPQ2d at 1228. The court further stated that the "range" disclosed in multiple prior art patents is "a distinction without a difference" from previous range cases which involved a range disclosed in a single patent since the "prior art suggested that a larger number of elongated grips in the weight plates was beneficial... thus plainly suggesting that one skilled in the art look to the range appearing in the prior art." Id.

Routine optimization is not considered inventive and no evidence has been presented that the selection of cycling performed was other than routine, that the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art. The prior art teaches the ability to perform Invader assays with no prior target amplification (see Fors) and Ohnishi teaches using 35 cycles. In the instant case the prior art discloses a range of 0-35 PCR cycles for Invader assays. Thus, using an intermediate number of cycles, namely 17 or fewer cycles would constitute routine optimization in the art.

Response to Arguments

The response traverses the rejection. The response asserts Fors teaches the complete avoidance of amplification cycles. This argument has been reviewed but

deemed not persuasive. Fors teaches the method can be performed without any amplification. Fors does not teach away and does not make any statements not to amplify. Fors teaches the Invader assay can be performed on unamplified DNA.

The response asserts that Ohnishi and Mein both teach the use of 35 cycles of amplification to reduce the amount of genomic DNA needed for genotyping. This argument has been considered but is not convincing because the level of skill in the art was extremely high. The examiner acknowledges Ohnishi and Mein both teach the use of 35 cycles of amplification prior to Invader assay detection.

Given the teachings in the art at the time the invention was made, the ordinary artisan would have appreciated you could have performed the method with no amplification, as well as 35 cycles of amplification. Given such a high level of skill in the art, the ordinary artisan would have a reasonable expectation of success that the Invader assay detection would have provided reliable results with a median number of cycles. The benefits and drawbacks for amplification are provided and well known in the art. The response, page 7, states that Ohnishi, Mein and Fors do not teach or suggest that fewer than 35 PCR cycles should or can be used. This statement is not supported by the evidence. Fors teaches Invader assay can be performed with 0, i.e. fewer than 35 PCR cycles. In other words, the art teaches Invader directed assay can be carried out with 35 cycles and with 0 cycles. It would have been well within the skill of the art to optimize the number of cycles between these two end points.

The response asserts Rameckers teaches away form the claimed invention and does not teach 17 cycles can be used. Taking a look at Figure 1, the ordinary artisan

can extrapolate, that in situations even with less than 1.0 amplification efficiency, such as 0.70 efficiency, lower number of cycles may be used with very large targets. As evidenced by Rameckers, the ordinary artisan could take the formula for evaluating the number of cycles and evaluate how much DNA was needed for how many cycles. The ordinary artisan would have been motivated to have optimized through routine experimentation the number of cycles to meet the needs of the particular amount of DNA available.

The response argues that only 2 nanograms of genomic DNA is used. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., only 2 nanograms of genomic DNA is used) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The response asserts that the number of cycles is directly linked to the advantages of PCR taught by Ohnishi and Mein and provides a table with yields after PCR. This argument has been reviewed but is not persuasive. The extraordinarily high state of the art for PCR amplification in 2003 outweighs any experimentation that may be required to evaluate the optimal number of PCR cycles for any particular amount of DNA. The ordinary artisan would weigh the benefits of increasing the cycles for PCR with the cross-contamination, infidelity drawbacks of PCR and would reach an optimal

result. The art teaches that with very large quantities of DNA, the number of cycles of PCR can be 17.

Thus for the reasons above and those already of record, the rejection is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claim 28, 33, 36-37, 43-44, 47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 10, 20-21 of U.S. Application No. 11/266,723. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim

is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, Claim 20, 21, 10 of U.S. Application No. 11/266,723 recites a method of

A method for multiplex detection of target nucleic acids, comprising: a) providing reverse transcription, polymerase chain reaction, and invasive cleavage assay reagents in a microfluidics card, wherein said reagents are configured to reverse transcribe, amplify, and detect said target nucleic acids; b) exposing a sample suspected of containing said target nucleic acids to said reagents using centrifugal force; and c) detecting the presence or absence of said target nucleic acids

Claim 21 requires less than 20 cycles of PCR.

Claim 10 is directed to blood samples.

The method of Claim 20 differs from Claim 28 herein in that it fails to disclose use of CFTR alleles for 17 PCR cycles. However, the portion of U.S. Application No. 11/266,723 that supports the use of CFTR alleles for 17 PCR cycles is found on pages 12 and 107. While the claims of '723 are directed to less than 20 cycles of PCR, the specification of '723 indicates that the preferred embodiments, the PCR reaction has less than 12 amplification cycles. Moreover, the specification of '723 provides an exemplary multiplex PCR combined with INVADER assay detection which is a 20-plex (pages 107-108 of '723). Therefore, it would have been obvious to modify the method of Claims 20, 21, 10 of U.S. Application No. 11/266,723 such that the ordinary artisan would have been motivated to have multiplexed the 20 alleles provided on page 107 using the preferred PCR cycles of 12.

Response to Arguments

The response traverses the rejection. The response asserts the double patenting rejections involve later filed applications and request the rejections be held in abeyance until such time as a claim is found to be allowable. This argument has been considered but is not convincing. MPEP provides guidance for setting forth provisional applications, as in this situation and the rejection has not been overcome. Thus for the reasons above and those already of record, the rejection is maintained.

11. Claim 30, 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 10, 20-21 of U.S. Application No. 11/266,723 in view of the Cystic Fibrosis Mutation Database (http://www.genet.sickkids.on.ca/cftr/app). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, Claim 20, 21, 10 of U.S. Application No. 11/266,723 recites a method of

A method for multiplex detection of target nucleic acids, comprising: a) providing reverse transcription, polymerase chain reaction, and invasive cleavage assay reagents in a microfluidics card, wherein said reagents are configured to reverse transcribe, amplify, and detect said target nucleic acids; b) exposing a sample suspected of

containing said target nucleic acids to said reagents using centrifugal force; and c) detecting the presence or absence of said target nucleic acids

Claim 21 requires less than 20 cycles of PCR.

Claim 10 is directed to blood samples.

The method of Claim 20 differs from Claim 30 herein in that it fails to disclose use of 30 CFTR alleles for 17 PCR cycles. However, the portion of U.S. Application No. 11/266,723 that supports the use of CFTR alleles for 17 PCR cycles is found on pages 12 and 107. While the claims of '723 are directed to less than 20 cycles of PCR, the specification of '723 indicates that the preferred embodiments, the PCR reaction has less than 12 amplification cycles. Moreover, the specification of '723 provides an exemplary multiplex PCR combined with INVADER assay detection which is a 20-plex (pages 107-108 of '723).

Moreover, the cystic fibrosis mutation databases teaches the collection of mutations in the CFTR gene. There are currently **1542** mutations listed in this CFTR mutation database. The mutations include SNPs and deletions. The most common F508 mutation is a deletion.

Therefore, it would have been obvious to modify the method of Claims 20, 21, 10 of U.S. Application No. 11/266,723 such that the ordinary artisan would have been motivated to have multiplexed the 30 alleles provided in the CFTR database using the preferred PCR cycles of 12.

Response to Arguments

The response traverses the rejection. The response asserts the double patenting rejections involve later filed applications and request the rejections be held in abeyance until such time as a claim is found to be allowable. This argument has been considered but is not convincing. MPEP provides guidance for setting forth provisional applications, as in this situation and the rejection has not been overcome. Thus for the reasons above and those already of record, the rejection is maintained.

12. Claim 28, 33, 36-37, 43-44, 47 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-7 of U.S. Application No. 10/967,711. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, Claim 1-7 of U.S. Application No. 10/967,711 recites a method of

> 1.A method for detecting a target nucleic acid in unpurified bodily fluids blood comprising: exposing a-n unpurified bodily fluid unpurified blood to detection assay reagents under conditions such that said target nucleic acid is detected, if present, in a single step reaction, wherein said detection assay reagents comprise a FEN-1 endonuclease, a thermostable DNA polymerase, and a buffer comprising TAPS.

2. The method of claim 1, wherein said single step reaction comprises a polymerase chain reaction.

3.The method of claim 1, wherein said single step reaction comprises a polymerase chain reaction and an invasive cleavage assay reaction.

6. The method of Claim 3, where said polymerase chain reaction has fewer than 15 amplification cycles.

The method of Claim 1 differs from Claim 28 herein in that it fails to disclose use of multiplex of CFTR alleles. However, the portion of U.S. Application No. 10/967,711 that supports the use of multiplex of CFTR alleles is found on page 105-107. While the claims of '711 are directed detecting a target nucleic acid the specification of '711 provides an exemplary multiplex PCR combined with INVADER assay detection which is a 20-plex (pages 105-107 of '711). Therefore, it would have been obvious to modify the method of Claims 1-7 of U.S. Application No 10/967,711 such that the ordinary artisan would have been motivated to have multiplexed the 20 alleles provided on page 107 to obtain simultaneous results.

Response to Arguments

The response traverses the rejection. The response asserts the double patenting rejections involve later filed applications and request the rejections be held in abeyance until such time as a claim is found to be allowable. This argument has been considered but is not convincing. MPEP provides guidance for setting forth provisional applications, as in this situation and the rejection has not been overcome. Thus for the reasons above and those already of record, the rejection is maintained.

13. Claim 30, 38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-7 of U.S. Application No. 10/967,711 in view of the Cystic Fibrosis Mutation Database (http://www.genet.sickkids.on.ca/cftr/app). An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by or would have been obvious over, the reference claim(s). See e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, Claim 1-7 of U.S. Application No. 10/967,711 recites a method of

> 1.A method for detecting a target nucleic acid in unpurified bodily fluids blood comprising: exposing a-n unpurified bodily fluid unpurified blood to detection assay reagents under conditions such that said target nucleic acid is detected, if present, in a single step reaction, wherein said detection assay reagents comprise a FEN-1 endonuclease, a thermostable DNA polymerase, and a buffer comprising TAPS.
>
> 2. The method of claim 1, wherein said single step reaction comprises a polymerase chain reaction.
>
> 3.The method of claim 1, wherein said single step reaction comprises a polymerase chain reaction and an invasive cleavage assay reaction.
>
> 6. The method of Claim 3, where said polymerase chain reaction has fewer than 15 amplification cycles.

The method of Claim 1 differs from Claim 28 herein in that it fails to disclose use of multiplex of CFTR alleles. However, the portion of U.S. Application No. 10/967,711 that supports the use of multiplex of CFTR alleles is found on page 105-107. While the claims of '711 are directed detecting a target nucleic acid the specification of '711 provides an exemplary multiplex PCR combined with INVADER assay detection which is a 20-plex (pages 105-107 of '711).

Moreover, the cystic fibrosis mutation databases teaches the collection of mutations in the CFTR gene. There are currently **1542** mutations listed in this CFTR mutation database. The mutations include SNPs and deletions. The most common F508 mutation is a deletion.

Therefore, it would have been obvious to modify the method of Claims 1-7 of U.S. Application No 10/967,711 such that the ordinary artisan would have been motivated to have multiplexed the 30 alleles provided in the cystic fibrosis mutation database to obtain simultaneous results.

Response to Arguments

The response traverses the rejection. The response asserts the double patenting rejections involve later filed applications and request the rejections be held in abeyance until such time as a claim is found to be allowable. This argument has been considered but is not convincing. MPEP provides guidance for setting forth provisional applications, as in this situation and the rejection has not been overcome. Thus for the reasons above and those already of record, the rejection is maintained.

Conclusion

14. **No claims allowable over the art.**

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (571) 272-0743. The examiner can normally be reached Monday-Friday from 7:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz, can be reached on (571)272-0763.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

The Central Fax Number for official correspondence is (571) 273-8300.

/Jeanine Goldberg/
Primary Examiner
June 24, 2009